

Atty. Dkt. No. 041673-2047

Clean Copy of the Amended Claims

1. A method for ameliorating neuronal atrophy and loss in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of the neurotrophin at, or within diffusion distance of, targeted cholinergic or dopaminergic neurons, wherein the neurotrophin is nerve growth factor (NGF) or glial derived nerve growth factor (GDNF) and stimulates non-chemotropic axonal growth by, or activity in, the targeted neurons.

Claims 2 through 5 are cancelled.

Claim 6 is withdrawn.

Claims 7 and 8 are cancelled.

Claims 9 and 10 are withdrawn.

Claims 11 through 20 are cancelled.

21. The method according to Claim 1, wherein the targeted neurons are cholinergic neurons.
22. The method according to Claim 21, wherein the stimulation occurs in a cortical region of the brain innervated by the targeted cholinergic neurons.
23. The method according to Claim 22, wherein each delivery site is preselected by correlating sites of potential loss of cortical fiber density to potential impairment of neurological function in the brain.
24. The method according to Claim 23, wherein the cortical region of the brain is the insular or temporal cortex.

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25. The method according to Claim 22, wherein the stimulation occurs in the cingulate, frontal, entorhinal or hippocampal cortices.

26. The method according to Claim 21, wherein the stimulation occurs in the cholinergic forebrain.

27. The method according to Claim 22 or 26, wherein the region of the brain containing the targeted neurons is the striatum.

28. The method according to Claim 26, wherein the treated mammal is a human with Alzheimer's Disease.

29. The method according to Claim 1, wherein the targeted neurons are dopaminergic neurons.

30. The method according to Claim 29, wherein the stimulation occurs in dopaminergic neurons innervating the substantia nigra.

31. The method according to Claim 30, wherein the region of the brain containing the targeted dopaminergic neurons is the striatum.

32. The method according to Claim 29, wherein the treated mammal is a human with Parkinson's Disease.

Claim 33 is cancelled.

34. The method according to Claim 1, wherein the growth factor-encoding transgene composition is delivered directly by introduction of a transgene-expressing recombinant expression vector into the preselected delivery sites.

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35. The method according to Claim 34, wherein the transgene-expressing recombinant expression vector is a viral vector.
36. The method according to Claim 35, wherein the viral vector is delivered in a pharmaceutically acceptable composition, and provides from 10^{10} to 10^{12} viral particles/ml of composition.
37. The method according to Claim 1, wherein the mammal is a human and the transgene encodes a human NGF or GDNF molecule.
38. The method according to Claim 37, wherein the transgene encodes human NGF.

Claim 39 is cancelled.

40. The method according to Claim 37, wherein the transgene encodes human GDNF.

Claims 41 through 43 are cancelled.

44. The method according to Claim 35, wherein the viral vector is an adeno-associated viral vector.
45. The method according to Claim 35, wherein the viral vector is a lentiviral vector.
46. The method according to Claim 1, wherein the mammal is a human with aging-related impairment.